

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No. : 10/573,129 Confirmation No. 8761
Applicant : Hansell H. Stedman et al.
371 Filed : March 23, 2006
Art Unit : 3767
Examiner : Bradley James Osinski
Customer No. : 00270
Title : METHODS, COMPOSITIONS AND APPARATUS FOR
DELIVERING HETEROLOGOUS MOLECULES TO CELLS

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Commissioner for Patents
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**SWORN DECLARATION UNDER 37 CFR 1.132
OF HANSELL H. STEDMAN
TRAVERSING REJECTION OF CLAIMS**

Sir:

I, Hansell H. Stedman, residing at 1907 Berks Road, Norristown, PA 19403, a citizen of the United States, and having been warned in accordance with Section 1001 of Title 18 of the United States Code, declare that:

1. I am a named joint inventor of the invention described in the above-identified

application.

2. My educational background and experience include:

Massachusetts Institute of Technology, Cambridge B,S, 1979 Biology & Chemistry

Harvard Medical School, Boston, MA M.D. 1984 Medicine/Genetics

University of Pennsylvania, Philadelphia, PA 1984-1994 Categorical General Surgery

Residency and Postdoctoral Fellowships in Human Genetics and Cell & Developmental Biology

3. I understand that independent claim 34 of the above referenced application is directed to “an internal occlusion balloon catheter for occluding blood flow through an aorta of a hypothermic patient” and requires “in an inflated condition, said balloon envelope forming an elongate, continuous, substantially-cylindrical tube along its full length, and when positioned within the patient’s aorta, said full length of said tube of said balloon envelope being of sufficient length to extend continuously from a location adjacent a bottom of the patient’s abdominal aorta through the patient’s aortic arch and into the patient’s ascending aorta thereby substantially filling and occluding flow within the patient’s entire aorta and preventing cross-flow through the aorta between various branch vessels branching from the aorta.”

4. I understand that independent claim 42 of the above referenced application is directed to “an internal occlusion balloon catheter for occluding blood flow through a vena cavae of a hypothermic patient” and requires “in an inflated condition, each of said series of balloons forming an elongate, continuous, substantially-cylindrical tube along its full length, and when positioned within the patient’s vena cavae, one of said balloons being of sufficient length to extend continuously from a location adjacent a lower end of the patient’s inferior vena cava to just below a right atrium of the patient’s heart and another one of said balloons being of sufficient length to extend through the patient’s superior vena cava and occlude the azygous vein but does not extend into the right atrium.”

5. Further, I understand that the Examiner has rejected the above claims and limitations as being obvious over U.S. Patent No. 5,728,066 to Daneshvar or as being obvious over Daneshvar in view of U.S. Patent No. 6,776,771 B2 issued to van Moorlegem. More specifically, I understand that the Examiner acknowledges that the above recited structural limitations with respect to the “length” of the elongate, continuous balloons of the catheters of the present invention are not disclosed by the cited references. However, I understand that the Examiner has taken the position that “it would have been an obvious matter of design choice to a person of ordinary skill in the art to modify the balloon of Daneshvar” to have the recited “length” limitation required by the claims of the above referenced application.

6. I respectfully submit that the structures defined by claims 34 and 42 of the above referenced application are not obvious over Daneshvar and Daneshvar in view of van Moorlegem et al. because modifying the catheters disclosed in these cited references according to the claimed invention of the above referenced application would result in the instantaneous fatality of the patient when used following the teachings of Daneshvar and/or van Moorlegem.

7. The present invention relates to gene therapy; Daneshvar and van Moorlegem do not. Daneshvar relates to a catheter used when monitoring pulsed blood flow of a warm patient through the heart of a patient (via injection of a contrast media directly into blood flow). Van Moorlegem relates to a dilation catheter used to widen a restricted blood flow passage.

8. According to the present invention, gene therapy is performed with the patient under total circulatory arrest and under hypothermic conditions. A region of the patient is isolated and exsanguinated. A macromolecular complex is delivered to the exsanguinated region and permitted to dwell within or extravasate from a contained portion of the vascular space for a predetermined period of time before being flushed of the region. The catheters of claims 34 and 42 of the above referenced application compartmentalize circulation in the central and peripheral vascular systems. The central circulation (i.e., vessels directly supplying the thoracic and abdominal viscera) is separated from the peripheral circulation (i.e., vessels supplying the skeletal muscles). When in the process of delivering a macromolecular complex, high venous pressure is applied and the inflated balloons transiently restrict flow of fluids between the peripheral and central circulations. Since the central vascular system includes vessels supplying the thoracic and abdominal viscera, transport of the complex to the abdominal viscera is minimized by restricting flow through the aorta and vena cavae, as they interconnect vessels supplying the thoracic and abdominal viscera.

9. An advantage provided by the catheters of the present invention is that the risk of side effects of gene therapy is reduced. The absence of circulating blood in the area to which the macromolecular complex is infused avoids contact with elements of the blood, such as cells, platelets, and tissue-reactive plasma components and minimizes the risk of inducing an immune response from circulating antibodies. The invention also minimizes activation of various clotting factors and other factors that may interfere with the transfer of the macromolecular complex.

Further, the catheters minimize, or eliminate, exposure of other non-targeted areas of the body to the complex, such as exposure of the macromolecular complex to the liver or lungs of the patient.

10. Daneshvar uses a balloon catheter to momentarily redirect or slow the flow of a material injected directly into pulsed blood flow in one location in the heart to prevent the material from quickly being washed out of the heart via pulsed blood flow. The momentary resistance created by the balloon also better disperses the injected material within the heart. Thus, one of ordinary skill in the art is taught a catheter structure for use in a warm patient under pulsed blood flow that enables the flow of blood through the heart to be better monitored (i.e., the injected material being a contrast media that can be imaged as it flows through the heart with pulsed blood flow).

11. The catheter of Daneshvar modified according to claims 34 or 42 of the above referenced application would be instantaneously lethal as used in accordance to Daneshvar and would destroy the intent, purpose and function of the catheter invention required of Daneshvar. Daneshvar's intention is not to entirely occlude flow through the entire aorta, prevent cross-flow between the aorta and branch vessels, or to entirely occlude the vena cavae. Rather, the balloon of Daneshvar is intended to momentarily redirect blood flow through the heart while still permitting normal pulsed blood flow to travel through the heart of the warm patient.

12. The catheter of van Moorlegem modified according to claim 42 of the above referenced application would be instantaneously lethal as used in accordance to van Moorlegem and would destroy the intent, purpose and function of the catheter invention required of van Moorlegem. Van Moorlegem's intention is not to entirely occlude flow through the entire aorta, prevent cross-flow between the aorta and branch vessels, or to entirely occlude the vena cavae. Rather, the balloon of van Moorlegem is for temporarily widening a restricted blood flow passage. Van Moorlegem discloses that "if the inflated balloon obstructs blood flow for too long (typically for more than a few seconds), permanent damage to downstream organs can occur" (see column 1, lines 54-60, of the van Moorlegem et al. patent and this is not even for a catheter deployed in the aorta or vena cavae).

13. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like are punishable by fine and imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful statements may jeopardize the validity of the application on any patent issued thereon.

Date: July 8, 2010

By: Hansell H. Stedman
Hansell H. Stedman

